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Non-Medical Management of Raynaud's Disease

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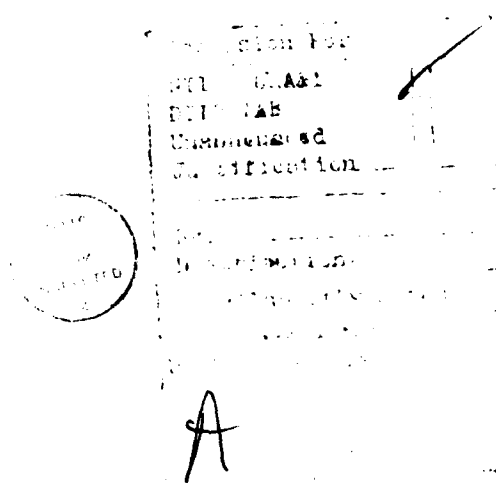
Running Head: Raynaud's Disease

ABSTRACT

This study examined the efficacy of a non-medical procedure for management of idiopathic Raynaud's disease. Individuals with Raynaud's disease and normal individuals were given 27 ten - minute simultaneous pairings of hand immersion in warm water (43°C) with a whole - body cold exposure (0°C). One group of normal and one group of subjects with Raynaud's disease received no treatments. Before and after cold test exposures (0°C) were given to all subjects. Subjects with Raynaud's disease receiving treatments demonstrated significant increases in digital temperatures compared to untreated subjects with Raynaud's disease during the cold test ($p < .05$). Treated and untreated normals did not differ from each other. Additionally, digital temperatures of treated subjects with Raynaud's disease increased to a level equal to that of normal subjects, although they demonstrated lower digital temperatures during initial cold exposure ($p < .01$). This therapy offers a practical alternative to traditional treatments with drugs or sympathectomy, without unwarranted side effects.



Raynaud's disease is generally defined as a primary (idiopathic) functional disease of the peripheral vasculature. The disease is characterized by vasospastic attacks accompanied by color changes (white pallor -- cyanotic blue -- deep red) of the affected digits.[1-4] These intermittent episodes are precipitated by exposure to cold or emotional distress. The vasospastic attacks are typically bilateral, usually involving the fingers or toes, and occasionally the ears and nose. When such attacks are secondary to obliterative vascular disease or collagen disease, they are referred to as Raynaud's phenomenon or syndrome. Minimal criteria for diagnosis of Raynaud's disease have long been established.[1,2,3,5,6]

Raynaud's disease has been commonly viewed as a disease of young women since 1932,[1,5] with emotional instability present in a large number of cases.[4] Medical treatment of the problem has changed very little over the ensuing years. Traditional treatments involve avoidance of the cold and emotional upset; the use of tranquilizers and vasodilating drugs; or in extreme cases, sympathectomy.[4]

There is controversy as to whether the etiology of Raynaud's disease is neurophysiological or metabolic.[7] According to the neurophysiological view, the disease appears to be a conditioning disturbance of the autonomic nervous system in which conditioning occurs easily or persists too long.[4] If this is the case, then alterations in nervous-system response to a cold stimulus should alter cold-sensitive symptomatology.

Experiments using biofeedback or autogenic training to counter-condition the autonomic-nervous-system response to cold have yielded mixed results.[8-10] Although significant warming of the hands has been demonstrated at warm room temperatures, there is little evidence that individuals with Raynaud's disease show improvement in a cold environment.

Pavlovian conditioning is an alternative method of counter-conditioning the autonomic nervous system. Research has shown that vasoconstriction and vasodilatation may be conditioned by Pavlovian methods.[11] Using these techniques it should be possible to alter the blood flow to the fingers increasing the digital temperatures in individuals with Raynaud's disease exposed to a cold environment. Preliminary work has indicated that such conditioning is helpful for individuals who are hypersensitive to cold.[12]

The purpose of the study was to explore the effects of Pavlovian conditioning with a view to increasing blood flow and subsequently measure an increase in digital temperature response to cold in individuals with primary Raynaud's disease using Pavlovian conditioning. To elicit increased temperatures, an unconditioned stimulus of warm water (43°C) to the hands was paired with a whole-body cold exposure (0°C) (conditioned stimulus). After repeated pairings exposure to cold air alone should elicit vasodilatation in the hands (conditioned response).

Method

Subjects: The study subjects were 36 men and women, 19-62 years of age, who volunteered from the local population and other laboratories. Subjects were modestly reimbursed for their participation. Eighteen of the subjects were diagnosed as suffering from primary Raynaud's disease, but were otherwise healthy. The other eighteen subjects demonstrated rewarming on a cold sensitivity test[13] and were in good health. One individual with Raynaud's disease and four normals did not complete the study because of absenteeism and nonrelated personal reasons and their data is not included in the analysis.

An interview/briefing was held with all volunteers, followed by a medical history and examination. During the interview the subject completed the IPAT

Anxiety Scale Questionnaire (ASQ)[15], the Eysenck Personality Questionnaire (EPQ)[16], a background questionnaire, and an environmental history questionnaire. In order to rule out possible complicating disease, and establish a diagnosis of primary Raynaud's disease, all individuals with suspected Raynaud's disease received the following blood tests: rheumatoid factor, cold agglutinins, cryoglobulins, sedimentation rate, antinuclear antibody, and serum glucose. Criteria for diagnosis of primary Raynaud's disease were those of Allen and Brown[6]. Individuals with hypertension and/or heart disease were excluded as a safety precaution. All subjects were then randomly assigned to either the treatment or the no-treatment group.

Instrumentation: The temperature response of the fingers to cold air before and after treatment (or no treatment) was measured by thermocouples attached to the dorsal aspect of each finger (excluding thumb) proximal to the nail bed. Each subject was also fitted with a thermocouple rectal probe and an eight-point thermocouple harness to determine a mean weighted skin temperature. The eight points were chest, lower back, abdomen, lateral upper arm, forehead, dorsal contralateral forearm, anterior thigh, and lateral calf. Temperatures were continuously monitored by a Leeds and Northrup Digimax Scanning Numatron and were collected by on-line computer with temperature recordings reported every 60 secs.

Warm water was provided by two Wide Range Laboratory Baths, Model 4-8600, manufactured by the American Instrument Co., Silver Springs, MD, each equipped with a plexiglass lid with two openings for the subjects' hands. Two in-house-fabricated hot-air baths were also used, each equipped with a Proportional Control, Model 72, manufactured by the Yellow Springs Instrument Co., Yellow Springs, OH.

Experimental Design: The experimental design of the study was a 2 x 2 randomized factorial blocks design[14] with one blocking variable (Raynaud's vs normal subjects) and one treatment variable (treatment vs no treatment). It was predicted that Raynaud's subjects given treatments would show a significant improvement in temperature response to cold relative to subjects with Raynaud's disease not given treatments. Normal subjects given treatments were not expected to experience significant changes in temperature relative to normal subjects serving as controls.

Procedure: The study was conducted during the months of October 1980, through March 1981, with treatments given on Mondays, Wednesdays, and Fridays, three per day, for three consecutive weeks. The week before treatments began all subjects (treated and not treated) received a test to determine their digital temperature response to cold. On these days the subjects were seated in a room at 23°C for thirty minutes in order to stabilize body temperatures. They then received a single 10-minute whole-body exposure to cold (0°C) dressed in indoor clothing (light coveralls and boots) seated on a stool with arms at heart level. The observed response on this cold test was the digital temperatures recorded during the last minute of the exposure. The cold test was repeated the week following the conclusion of treatments to establish changes in the response to cold exposure of both treated and non-treated groups.

On each treatment day the subjects received three treatment trials. Upon arrival at the chambers building the subjects changed into the coveralls and boots, and were then instrumented with thermocouples. Prior to entering the cold chamber, the subjects sat in a warm room (23°C) and placed their hands in a box containing warm circulating air (49°C) to induce vasodilatation. Subjects then entered the cold chamber (0°C) and placed their hands in a water bath (43°C) for 10 minutes. After each treatment the subjects were removed from

the cold chamber for five minutes and placed their hands in the warm air box. The procedure was repeated twice for a total of three trials. Finally, the subject's temperatures at room temperature (23°C) were monitored for five minutes. Subjects in the no-treatment control groups participated only in the cold tests prior to and after treatment phases.

Statistical Analysis: All data analyses were conducted using mean digital temperatures at the end of cold exposure of the dominant hand as the dependent measure. Data were analyzed using a 2 x 2 analysis of covariance (ANCOVA) with subject's digital temperature on the pre-treatment cold exposure as the covariate and the temperature on the post-treatment cold exposure as the dependent variable. Differences between groups were then computed using the error term from the ANCOVA utilizing Duncan's Multiple-Range Test for Nearly Equal Ns.[17] Comparisons were performed on pre-treatment data using student t-tests.

Results

Treated individuals with Raynaud's diesease showed significant improvement in their condition when compared with untreated individuals with Raynaud's disease. These subjects had superior digital temperatures after 10 minutes exposure to 0°C ($p < .05$), as can be seen in Figure 1. Furthermore, the digital temperatures of treated Raynaud's afflicted subjects were not different from that of normal subjects on the post treatment cold test. There were, however, considerable differences between Raynaud's afflicted and normal subjects on the pretest ($p < .01$). Treatments appeared to result in long lasting benefits for Raynaud's afflicted individuals. Several of these subjects were retested up to four months after the treatments and all maintained improvement in their response to cold.

FIGURE 1 ABOUT HERE

Treatments did not result in improvement in the digital cold response for normal subjects. Digital temperatures of treated and not treated normal subjects did not differ from each other on the post test, as can be seen in Figure 1.

Raynaud's afflicted subjects demonstrated lower digital temperatures (27.3°C) than normals (33.3°C) ($p < .01$) at room temperature (23°C) consistent with the previous findings of Peacock.[18] Resting digital temperatures of both normal and Raynaud's afflicted subjects were higher than that reported by Peacock. However, the ambient (room) temperature in the present study was 23°C and the room temperature in the Peacock study was 20°C.

There was no evidence in the present study that individuals with Raynaud's disease are less emotionally stable than the general population. Anxiety scores of subjects with Raynaud's disease on the ASQ (25.8) did not differ significantly either from the normal subjects (27.4) or from the norms of the test (27.1). Likewise, Raynaud's afflicted subjects did not differ on emotionality as measured by the "neuroticism" scale of the EPQ. Scores of subjects with Raynaud's disease (10.40) did not differ significantly either from the scores of normal subjects (8.20) or from the adult test norms (8.51 - 13.28).

Raynaud's afflicted subjects in the treatment group reported improvements in their condition. The most frequent comments were that their hands returned to normal much faster after episodes of vasospasm and that their hands felt much warmer. Others stated that they no longer wore gloves to shovel snow, to drive on cold days, or to go outdoors in the cold. Still others reported that their attacks now occurred less frequently and were less severe.

Case 1: A 34 year old male engineer had suffered from Raynaud's disease for 15 years. When he arrived for his physical, he removed his gloves and his fingers were white to the proximal interphalangeal joint. He had previously participated in a study of autogenic training[10] and reported that his condition was not improved as a result. One of his parents suffered from Raynaud's disease. He described his attacks as very severe and that they were caused by chilling of hands only, chilling of body, or by anxiety (psychological tests suggests that he is not an anxious person). He was not taking any medications and was a nonsmoker. Physical examination and blood work were unremarkable. After four days of conditioning treatments, he reported that he was "feeling better". Two days later, he reported that his left hand and two fingers on his right hand were "100% improved "and that his hands felt "hot". His improvement in average finger temperature of the dominant hand was 4.2°C during the post-test cold exposure.

Case 2: A 54 year old female had suffered from Raynaud's disease for 10 years. She had spent the majority of her life in Alabama but was now living in the Boston area. Upon her arrival at the interview, her fingers were white to the proximal interphalangeal joint, although she was wearing gloves. She described her attacks as very severe and very painful, with all fingers involved. She appeared to have very severe vasospastic episodes. She stated that her attacks were caused by ambient temperature changes, touching cold objects, and body chilling. Physical examination and blood work were unremarkable, and her psychological tests revealed nothing unusual. She took butabarbital and belladonna extract daily and did not smoke. During the treatment sessions, her body appeared to be shivering and she reported that she was very cold. Following the series of 27 treatments, she showed no improvement. A second series of 27 treatments was then instituted after which she demonstrated very

significant improvement in her condition (data not used in analysis). Digital temperature of her dominant hand increased 6.0°C during the post test after the second series.

Discussion

Raynaud's afflicted subjects demonstrated substantially lower digital temperatures at room temperature than normal subjects. This finding is consistent with the results of Peacock[18], indicating that digital temperatures may be a useful tool in diagnosing peripheral vascular diseases such as Raynaud's disease. This result also supports Peacock's contention that an attenuation of peripheral circulation exists in such individuals, even at higher temperatures.

As a result of a simple Pavlovian therapy, individuals with Raynaud's disease demonstrated beneficial increases in digital temperature response to cold. Moreover, their improvement was to a level equal to that of normal subjects. These results suggest that classical conditioning therapy is a feasible alternative to the more traditional medical management techniques. Conditioning therapy avoids the problem of side effects of drugs and the loss of nerve function secondary to sympathectomy. The classical conditioning procedure does not require expensive equipment, and could be therapeutically applied safely and economically using commercially available or fabricated temperature regulated water baths and naturally occurring ambient cold.

These results also compare quite favorably with results obtained using biofeedback with several important advantages. First, in the present study Raynaud's afflicted subjects demonstrated improved digital temperatures during cold exposure of 0°C, whereas most biofeedback studies report results under relatively mild conditions. Secondly, improvements in Raynaud's episodes reported in biofeedback studies are largely subjective, with little or no objective

measure to verify positive results in response to cold. Thirdly, biofeedback usually requires "suggestive" subjects implying a placebo effect.

Finally, Pavlovian conditioning seems to be more robust than other therapies in that it appears to be applicable to a wider range of individuals and has a more prolonged effect. The results of the present study are consistent with earlier basic research[11], and provide promise to a large number of individuals who suffer from various forms of cold hypersensitivity.

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Footnotes

Jared B. Jobe, James B. Sampson, and Donald E. Roberts are from the US Army Research Institute of Environmental Medicine, Natick, MA, and William P. Beetham, Jr. is from the Lahey Clinical Medical Center, Burlington, MA.

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All subjects participated in this study after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Reg. 70-25 on Use of Volunteers in Research.

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy, or decision, unless so designated by other official documentation.

Figure Captions

Figure 1. Mean digital temperatures of treated and not treated (control) subjects with Raynaud's disease and normals.

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This study examined the efficacy of a non-medical procedure for management of idiopathic Raynaud's disease. Raynaud's and normal individuals were given 27 ten-minute simultaneous pairings of hand immersion in warm water (43°C) with a whole-body cold exposure (0°C). One group of normal and one group of Raynaud's subjects received no treatments. Before and after cold test exposures (0°C) were given to tall subjects. Raynaud's subjects receiving treatments demonstrated significant increases in digital temperatures compared to untreated

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Raynaud's subjects during the cold test ($p<.05$). Treated and untreated normals did not differ from each other. Additionally, digital temperatures of treated Raynaud's subjects increased to a level equal to that of normal subjects, although they demonstrated lower digital temperatures during initial cold exposure ($p<.01$). This therapy offers a practical alternative to traditional treatments with drugs of sympathectomy, without unwarranted side effects.